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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/905,449	07/13/2001	Avi Ashkenazi	10466/58	1667

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EXAMINER
MOSHER, MARY

ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 10/02/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/905,449	Applicant(s) Askenazi et al
	Examiner Mosher	Art Unit 1648

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *1/22/2002, 3/28/2002, 3/25/2002, 7/13/2001, 8/27/2002* .

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *39-51* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *39-51* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). *6, 8*
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Claim Rejections - 35 USC § 112

Claims 39-44, 47, 48, 50, and 51 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. These claims recite "extracellular domain." Figure 17 teaches a polypeptide of 390 amino acids, with a signal peptide at amino acids 1-29 and a transmembrane domain at amino acids 245-267. Although the rest of the polypeptide falls into two domains which lie on either side of the transmembrane domain, the specification does not teach which of the two domains is "extracellular". Therefore it is unclear what segment of the polypeptide is the "extracellular domain."

Claims 39-44 and 46-51 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated polypeptide having at least 85% sequence identity to the polypeptide of SEQ ID NO:39 or polypeptide lacking the signal peptide, which isolated polypeptide inhibits VEGF-stimulated epithelial cell growth, the specification does not reasonably provide enablement for a polypeptide which does not have this activity. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. Claims 39-44 and 46-51 are drawn to polypeptides comprising the sequence shown in Figure 17 (SEQ ID NO:39, PRO246), or to its "extracellular domain", or to signal-sequence-free forms, or to the

protein encoded by the original cloned DNA, or to variants at with least 85% identical amino acid sequence of any of these. The claims do no contain any functional limitation.

The specification identifies PRO246 as a membrane-bound polypeptide having homology to the human Coxsackie-adenovirus receptor and to various tumor antigens, and puts forth several possible uses: as a possible receptor for one or more viruses, or possible use as a tumor antigen. On pages 204-205, the specification teaches that PRO246 has a specific biological activity, inhibiting VEGF-stimulated epithelial cell proliferation. While one of skilled in the art would be able, without undue experimentation, to use polypeptides with this biological activity, the specification does not adequately teach how to use PRO246 derivatives without this biological activity. Regarding use as a virus receptor, in the absence of information on which viruses, if any, actually use the protein as a receptor, it would require undue experimentation to use the protein in the manner suggested for a virus receptor. In regard to use as a tumor antigen, on page 244, analysis of the expression of PRO246 concludes that the protein is expressed in certain fetal and adult tissues, especially fetal vascular endothelium, and not obviously expressed at higher levels in tumor vascular endothelium. Therefore, in the absence of teachings on the actual appearance of the protein as an antigen in tumors and evidence of diagnostic or therapeutic usefulness regarding tumors, it would require undue experimentation to use the protein in the manner suggested for a tumor antigen. In conclusion, because of the very limited teachings and absence of working examples for any of the alternative uses of the polypeptide, the absence of teachings for how to use variants of the polypeptide which lack the demonstrated anti-VEGF activity, and the large

quantity of experimentation required to find a use for polypeptides with unknown biological activity, it is concluded that enablement is limited to those structural variants which inhibit VEGF-stimulated epithelial cell growth.

Claims 39-44, 50, 51 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claims 39-44, 50, 51 are drawn to polypeptides having at least 85%, 90%, 95% or 99% sequence identity with a particular disclosed sequence. The claims do not require that the polypeptide possess any particular biological activity, nor any particular conserved structure, or other disclosed distinguishing feature. Thus, the claims are drawn to a genus of polypeptides that is defined only by sequence identity.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of compete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factor present in the claim is a partial structure in the form of a recitation of percent identity. There is not even identification of any particular portion of the structure that must be conserved. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of polypeptides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See Fiers v. Revel, 25 USPQ2d 1601 at 1606 (CAFC 1993) and Amgen Inc. v. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016.

One cannot describe what one has not conceived. See Fiddes v. Baird, 30 USPQ2d 1481 at 1483. In Fiddes, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only isolated polypeptides comprising the amino acid sequence set forth in SEQ ID NO: 39, but not the full breadth of the claim meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that Vas-Cath makes clear that the

written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (e) the invention was described in-
> (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effect under this subsection of a national application published under section 122(b) only if the international application designating the United States was published under Article 21(2)(a) of such treaty in the English language; or
> (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that a patent shall not be deemed filed in the United States for the purposes of this subsection based on the filing of an international application filed under the treaty defined in section 351(a).

Claims 39-46, 49, 50 are rejected under 35 U.S.C. 102(e2) as being anticipated by Lal et al 5,942,606.

In making this rejection, applicants are denied the benefit of priority applications PCT/US98/18824 and US 60/062816. As discussed above, the disclosure regarding PRO246 as a possible virus receptor or a possible tumor antigen does not enable one skilled in the art to use the protein, without undue experimentation. Since the anti-VEGF biological activity which enables one skilled in the art to use the protein is first disclosed in PCT/US98/19330, the effective date of this application is seen as 9/16/1998. Lal et al teaches a polypeptide, ACVRP, which is 100% identical to SEQ ID NO:39, see SEQ ID NO:1. Lal also teaches producing the protein in a host cell for post-translational processing to cleave a prepro form, see column 15 lines 17-32, and

teaches fusion proteins, see column 17, lines 1-34, thereby meeting each and every claim limitation.

Information Disclosure Statement

The index to the file contents indicates that an IDS was filed 7/13/2001. Is this correct? Could applicant supply a replacement copy? The examiner is unable to find an IDS with this filing date.

The following documents are cited as of interest, in disclosing polypeptides similar to or identical to SEQ ID NO:39. Copies are not provided, since each is exceedingly bulky.

Reference	Protein
WO200011015	vc51-1, SEQ 38
EP1067182	PSEC0086, SEQ 84
Reference	Protein
WO200149728, US20020061567	HP10801
WO200125427	Human shear stress-response protein SEQ 144.
WO9958660	gene 29
WO200078808, US6406884	INTERCEPT 258, SEQ 28.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mary E. Mosher, Ph.D. whose telephone number is (703) 308-2926. The examiner can normally be reached on Monday -Thursday and alternate Fridays from 6:30 AM to 4:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel, can be reached on (703) 308-4027. The fax phone number for this Group is now (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

September 30, 2002

MARY E. MOSHER
PRIMARY EXAMINER
GROUP ~~1800~~ 1600